メタリルクロライドのラット及びマウスを用いた
吸 入 に よ る が ん 原 性 予 備 試 験 報 告 書

試験番号

13 週間試験：ラット/0208；マウス/0209

APPENDIX

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX B 1-1

CLINICAL OBSERVATION (THIRTEEN-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 0-0 1	1-7 1	2-7 1	3-7 1	4-7 1	5-7 1	6-7 1	7-7 1	8-7 1	9-7 1	10-7 1	11-7 1	12-7 1	13-6 1
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	31 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	63 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	125 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	1	0	0	0	0	0	0	0	0
PARALYTIC GAIT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	31 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	63 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	125 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	1	0	0	0	0	0	0	0	0
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	31 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	63 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	125 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	1	0	0	0	0	0	0	0	0
IRREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	31 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	63 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	125 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	1	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	31 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	63 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	125 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	1	0	0	0	0	0	0	0	0

Clinical sign	Group Name	Administration Week-day 13-7 1
LOCOMOTOR MOVEMENT DECR	Control	0
	31 ppm	0
	63 ppm	0
	125 ppm	0
	250 ppm	0
	500 ppm	0
PARALYTIC GAIT	Control	0
	31 ppm	0
	63 ppm	0
	125 ppm	0
	250 ppm	0
	500 ppm	0
SOILED PERI GENITALIA	Control	0
	31 ppm	0
	63 ppm	0
	125 ppm	0
	250 ppm	0
	500 ppm	0
IRREGULAR BREATHING	Control	0
	31 ppm	0
	63 ppm	0
	125 ppm	0
	250 ppm	0
	500 ppm	0
ABNORMAL RESPIRATION	Control	0
	31 ppm	0
	63 ppm	0
	125 ppm	0
	250 ppm	0
	500 ppm	0

APPENDIX B 1-2

CLINICAL OBSERVATION (THIRTEEN-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-6
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	31 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	63 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	125 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	0	0	0	1	1	1	1	1	0
EYE OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	31 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	63 ppm	0	0	0	0	0	0	0	0	0	0	1	1	1	1
	125 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 13-7 1
SOILED	Control	0
	31 ppm	0
	63 ppm	0
	125 ppm	0
	250 ppm	0
	500 ppm	0
EYE OPACITY	Control	0
	31 ppm	0
	63 ppm	1
	125 ppm	0
	250 ppm	0
	500 ppm	0

APPENDIX B 2-1

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0208
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	120± 5	144± 8	172± 14	192± 18	219± 19	240± 19	257± 20
31 ppm	120± 4	143± 7	170± 10	188± 12	214± 16	230± 18	245± 18
63 ppm	120± 5	144± 8	171± 12	189± 14	211± 15	228± 14	244± 11
125 ppm	120± 5	145± 8	172± 12	188± 17	208± 18	224± 20	240± 20
250 ppm	120± 4	139± 5	165± 10	180± 12	199± 14*	214± 14**	226± 15**
500 ppm	121± 5	127± 7**	148± 9**	154± 9**	165± 13**	158± 12**	156± 21**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0208
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-6
Control	271± 20	285± 21	299± 21	311± 22	321± 23	328± 24	331± 25
31 ppm	260± 19	273± 19	284± 21	292± 20	302± 21	309± 21	315± 22
63 ppm	259± 12	273± 14	285± 15	295± 16	305± 16	313± 17	319± 17
125 ppm	255± 21	268± 21	282± 21	292± 21	301± 22	310± 22	314± 23
250 ppm	240± 14**	254± 14**	266± 14**	277± 14**	286± 14**	296± 14**	302± 13**
500 ppm	163± 10**	172± 9**	181± 11**	184± 12**	180± 14**	173± 14**	174± 15**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 2-2

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0208
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	98± 3	111± 2	124± 4	129± 4	141± 7	148± 8	153± 9
31 ppm	98± 3	110± 5	126± 6	131± 6	144± 7	150± 7	157± 7
63 ppm	98± 3	111± 4	126± 4	133± 7	143± 7	153± 8	156± 8
125 ppm	98± 3	112± 4	128± 5	134± 5	145± 5	150± 6	157± 7
250 ppm	98± 3	108± 3	122± 4	128± 5	137± 5	144± 7	150± 5
500 ppm	98± 3	101± 3**	114± 5**	117± 5**	123± 6**	121± 5**	124± 8**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0208
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-6
Control	159± 9	165± 7	170± 8	175± 9	180± 9	184± 9	183± 8
31 ppm	162± 8	167± 8	171± 9	175± 9	180± 9	186± 11	185± 10
63 ppm	163± 8	166± 8	169± 9	173± 9	178± 10	182± 11	183± 11
125 ppm	162± 8	166± 8	171± 9	175± 10	179± 11	181± 11	183± 12
250 ppm	156± 7	160± 8	164± 8	167± 8	172± 9	177± 9	177± 8
500 ppm	124± 13**	125± 12**	128± 11**	129± 12**	128± 12**	127± 14**	127± 14**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 2-3

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	22.8± 1.0	24.3± 1.2	25.3± 1.2	25.8± 1.3	26.2± 1.1	27.4± 1.3	28.3± 1.3
31 ppm	22.6± 0.8	23.8± 1.2	24.5± 1.3	25.2± 1.6	25.5± 1.7	26.3± 1.9	26.9± 2.1
63 ppm	22.6± 0.9	23.9± 1.1	24.6± 1.2	25.4± 1.6	25.8± 2.0	26.5± 2.0	27.2± 2.3
125 ppm	22.6± 1.0	23.7± 1.2	24.5± 1.3	24.6± 1.2	25.3± 1.1	25.8± 1.4	26.3± 1.2
250 ppm	22.5± 0.8	23.3± 1.1	24.2± 1.1	24.7± 1.1	25.4± 1.3	25.4± 1.1	26.5± 1.5
500 ppm	22.6± 1.1	-	-	-	-	-	-

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-6
Control	29.3± 1.7	30.0± 1.7	30.8± 1.9	31.4± 1.8	32.2± 2.1	32.0± 3.4	32.8± 2.5
31 ppm	28.1± 2.0	28.2± 2.2	28.6± 2.0	29.3± 2.3	30.0± 2.2	30.5± 2.3	31.3± 2.4
63 ppm	27.9± 2.4	28.6± 2.4	29.4± 2.7	29.7± 2.5	30.4± 2.5	30.7± 2.6	31.2± 2.6
125 ppm	27.3± 1.7	27.4± 1.9	27.9± 1.9**	28.0± 1.6**	28.4± 1.6**	28.6± 2.0*	29.6± 1.9*
250 ppm	27.3± 1.3	26.7± 2.9**	27.9± 1.2**	28.3± 1.4**	28.8± 1.5**	29.5± 1.7	29.6± 1.6*
500 ppm	-	-	-	-	-	-	-

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 2-4

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	18.4± 0.8	19.9± 1.0	20.4± 0.9	21.1± 0.8	21.5± 1.3	22.2± 0.8	22.7± 1.0
31 ppm	18.2± 1.1	19.6± 1.1	20.2± 1.0	21.1± 1.2	21.7± 1.2	22.2± 1.3	22.4± 1.4
63 ppm	18.2± 0.8	19.4± 1.3	20.0± 0.9	20.8± 1.0	21.2± 0.7	21.9± 1.0	22.4± 1.1
125 ppm	18.2± 0.6	19.6± 1.0	20.3± 0.7	20.6± 1.0	21.3± 1.2	22.0± 1.0	21.9± 1.0
250 ppm	18.3± 0.6	19.5± 0.8	19.9± 0.5	20.8± 0.6	21.5± 0.9	21.7± 0.8	21.7± 0.7
500 ppm	18.3± 0.8	14.7± 3.6 ?	19.0± 0.0 ?	19.0± 0.0 ?	20.0± 0.0 ?	19.6± 0.0 ?	20.7± 0.0 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-6
Control	23.3± 1.0	23.7± 1.3	23.8± 1.1	23.8± 1.6	24.4± 1.1	24.3± 1.4	25.0± 1.7
31 ppm	23.4± 1.9	24.2± 1.8	24.1± 1.6	24.0± 1.8	24.3± 1.6	24.7± 2.0	24.8± 2.3
63 ppm	23.2± 0.9	23.5± 1.0	23.4± 1.3	23.5± 1.3	24.0± 1.0	24.3± 1.3	24.5± 1.2
125 ppm	23.1± 1.0	23.1± 1.2	23.0± 1.5	23.7± 1.2	24.1± 1.5	24.4± 1.1	23.9± 1.1
250 ppm	22.8± 0.7	23.1± 0.8	23.0± 0.8	23.4± 0.9	24.1± 0.8	24.0± 1.1	24.2± 0.9
500 ppm	21.6± 0.0 ?	21.9± 0.0 ?	21.6± 0.0 ?	21.8± 0.0 ?	22.1± 0.0 ?	22.5± 0.0 ?	22.3± 0.0 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX B 3-1

FOOD CONSUMPTION CHANGES: SUMMARY, RAT: MALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0208
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	14.1± 0.7	15.3± 1.3	15.8± 1.8	16.5± 2.0	17.6± 1.3	17.4± 1.3	17.6± 1.2
31 ppm	13.9± 0.4	15.2± 0.9	15.3± 1.1	15.7± 1.5	16.6± 1.8	16.3± 1.6	16.9± 1.2
63 ppm	14.2± 0.9	15.7± 1.0	16.0± 1.1	15.4± 1.3	15.9± 1.4	16.3± 0.9	16.7± 1.1
125 ppm	13.6± 0.7	16.0± 1.0	15.2± 1.6	15.1± 1.6	15.5± 1.8*	15.6± 1.6	16.1± 1.6
250 ppm	12.6± 0.6**	15.4± 0.9	14.4± 1.4	15.1± 1.1	15.4± 1.1*	15.5± 1.4	15.9± 1.0
500 ppm	11.6± 1.3**	15.0± 1.4	14.2± 1.0*	14.7± 1.6	12.9± 2.7**	11.6± 3.7**	9.4± 4.6**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0208
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-6(6)
Control	17.4± 1.1	17.9± 1.3	17.7± 1.1	17.7± 1.3	17.6± 1.5	16.1± 1.4
31 ppm	16.6± 1.3	16.9± 1.3	16.2± 1.4*	16.5± 1.3	16.5± 1.3	15.4± 1.2
63 ppm	16.8± 1.3	17.2± 1.4	16.7± 1.3	17.3± 1.2	17.1± 1.6	16.8± 0.9
125 ppm	16.5± 1.3	17.0± 1.4	16.5± 1.1	16.5± 1.1	16.3± 1.2	16.3± 1.2
250 ppm	16.2± 1.0	16.7± 0.7	16.4± 0.7	16.7± 0.9	16.6± 0.7	16.9± 0.7
500 ppm	13.2± 1.2**	13.8± 1.2**	13.8± 1.0**	13.7± 1.1**	11.3± 1.8**	11.1± 4.5**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 3-2

FOOD CONSUMPTION CHANGES: SUMMARY, RAT: FEMALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0208
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	11.2± 0.5	11.8± 0.6	11.4± 0.7	11.4± 0.9	11.8± 1.3	11.4± 0.9	11.8± 1.2
31 ppm	11.3± 0.5	12.2± 0.6	12.0± 1.0	11.6± 0.8	12.6± 1.1	12.0± 1.0	12.1± 0.9
63 ppm	11.6± 0.9	12.4± 0.9	12.5± 1.5	11.7± 1.1	12.6± 1.4	11.7± 1.1	11.7± 0.6
125 ppm	11.7± 1.0	13.3± 0.6**	12.2± 1.1	11.7± 0.7	12.0± 1.2	12.0± 1.6	11.8± 1.3
250 ppm	10.8± 0.4	12.4± 0.6	10.9± 0.9	11.8± 0.5	11.7± 0.6	11.6± 0.7	11.6± 0.6
500 ppm	9.9± 0.7**	11.9± 0.8	11.6± 0.8	12.2± 0.8	12.1± 0.9	10.8± 2.9	11.0± 2.3

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0208
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-6(6)
Control	11.6± 0.4	11.7± 0.9	11.5± 1.0	11.6± 1.0	11.9± 0.8	10.6± 0.7
31 ppm	11.6± 0.8	12.0± 0.9	11.3± 0.8	11.4± 1.3	12.2± 1.5	10.9± 1.1
63 ppm	11.3± 0.6	11.2± 1.0	11.0± 1.0	11.4± 0.8	11.4± 1.0	10.6± 0.6
125 ppm	11.5± 1.2	11.5± 1.2	11.2± 1.3	11.4± 1.1	11.2± 1.1	11.2± 1.1
250 ppm	11.3± 0.9	11.2± 0.9	11.0± 0.7	11.0± 1.0	11.8± 1.2	11.2± 1.0
500 ppm	11.2± 1.2	11.2± 1.2	10.2± 0.8	11.1± 1.1	10.4± 1.2*	9.2± 1.7

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 3-3

FOOD CONSUMPTION CHANGES: SUMMARY, MOUSE: MALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	4.1± 0.3	4.0± 0.2	4.1± 0.2	4.2± 0.2	4.2± 0.2	4.4± 0.2	4.5± 0.3
31 ppm	4.1± 0.2	4.1± 0.2	4.1± 0.3	4.3± 0.2	4.4± 0.2	4.3± 0.3	4.4± 0.3
63 ppm	4.0± 0.2	3.9± 0.2	4.1± 0.3	4.3± 0.3	4.4± 0.3	4.5± 0.3	4.5± 0.4
125 ppm	3.7± 0.2*	4.1± 0.4	4.0± 0.5	4.3± 0.5	4.2± 0.5	4.3± 0.4	4.4± 0.4
250 ppm	3.9± 0.2	4.0± 0.2	3.9± 0.3	4.1± 0.2	4.1± 0.2	4.3± 0.2	4.3± 0.2
500 ppm	0.1± 0.2**	-	-	-	-	-	-

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-6(6)
Control	4.5± 0.3	4.7± 0.2	4.5± 0.3	4.5± 0.3	4.4± 0.8	4.3± 0.3
31 ppm	4.3± 0.3	4.5± 0.3	4.5± 0.2	4.5± 0.3	4.4± 0.4	4.3± 0.4
63 ppm	4.5± 0.4	4.7± 0.4	4.6± 0.4	4.5± 0.3	4.5± 0.4	4.3± 0.3
125 ppm	4.5± 0.5	4.5± 0.4	4.2± 0.4	4.3± 0.4	4.2± 0.3	4.2± 0.3
250 ppm	4.0± 0.8	4.6± 0.7	4.2± 0.1*	4.3± 0.2	4.3± 0.2	4.1± 0.2
500 ppm	-	-	-	-	-	-

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX 3-4

FOOD CONSUMPTION CHANGES: SUMMARY, MOUSE: FEMALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	3.6± 0.2	3.6± 0.2	3.8± 0.2	3.9± 0.2	3.9± 0.2	4.1± 0.4	4.3± 0.2
31 ppm	3.5± 0.2	3.5± 0.3	3.7± 0.2	3.9± 0.2	3.9± 0.3	4.0± 0.3	4.2± 0.3
63 ppm	3.6± 0.2	3.7± 0.1	3.9± 0.1	4.0± 0.1	4.1± 0.2	4.3± 0.2	4.5± 0.2
125 ppm	3.5± 0.3	3.7± 0.2	3.7± 0.3	3.8± 0.2	3.9± 0.2	4.0± 0.3	4.2± 0.3
250 ppm	3.2± 0.2*	3.4± 0.2*	3.5± 0.2*	3.7± 0.2	3.6± 0.2*	3.7± 0.2*	3.8± 0.4**
500 ppm	0.6± 0.9**	2.9± 1.5 ?	3.3± 0.0 ?	4.0± 0.0 ?	3.7± 0.0 ?	3.9± 0.0 ?	3.8± 0.0 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-6(6)
Control	4.4± 0.3	4.5± 0.3	4.4± 0.4	4.4± 0.3	4.3± 0.3	4.4± 0.3
31 ppm	4.2± 0.3	4.1± 0.3*	4.0± 0.4	4.1± 0.3*	4.1± 0.4	4.0± 0.4
63 ppm	4.5± 0.2	4.6± 0.3	4.4± 0.2	4.5± 0.2	4.4± 0.2	4.2± 0.3
125 ppm	4.3± 0.4	4.4± 0.3	4.2± 0.3	4.2± 0.3	4.1± 0.2	4.0± 0.4*
250 ppm	3.8± 0.2**	3.8± 0.3**	3.8± 0.3**	3.9± 0.2**	3.9± 0.3*	3.7± 0.3**
500 ppm	3.8± 0.0 ?	3.7± 0.0 ?	3.6± 0.0 ?	3.7± 0.0 ?	3.8± 0.0 ?	3.5± 0.0 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX B 4-1

HEMATOLOGY (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : MALE

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	9.57± 0.15	16.3± 0.3	47.0± 1.2	49.2± 0.7	17.1± 0.2	34.7± 0.3	773± 23
31 ppm	10	9.57± 0.33	16.4± 0.3	47.1± 1.7	49.2± 0.4	17.2± 0.4	34.9± 0.8	756± 32
63 ppm	10	9.66± 0.19	16.4± 0.4	47.3± 0.9	49.0± 0.5	17.0± 0.3	34.6± 0.6	762± 39
125 ppm	10	9.68± 0.20	16.5± 0.4	47.5± 1.2	49.0± 0.7	17.0± 0.3	34.7± 0.5	827± 129
250 ppm	10	9.50± 0.17	16.4± 0.2	47.4± 1.2	49.9± 0.6	17.2± 0.2	34.6± 0.6	813± 34
500 ppm	6	8.17± 0.33**	14.6± 0.6**	42.9± 1.4**	52.6± 1.1**	17.9± 0.4**	34.1± 0.8	831± 85

Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$ Test of Dunnett

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	10	4.88± 2.01	0± 1	30± 5	2± 1	0± 0	4± 2	64± 6	0± 0
31 ppm	10	4.84± 1.43	0± 1	29± 7	1± 1	0± 0	5± 2	65± 7	0± 0
63 ppm	10	5.28± 1.82	1± 1	28± 5	1± 1	0± 0	4± 1	66± 5	0± 0
125 ppm	10	6.10± 1.80	0± 1	30± 5	2± 1	0± 0	5± 1	64± 6	0± 0
250 ppm	10	5.69± 1.58	0± 0	27± 4	1± 1	0± 0	4± 1	68± 4	0± 0
500 ppm	6	2.83± 0.70	1± 1	43± 8**	2± 1	0± 0	4± 2	51± 7**	0± 0

Significant difference : * : $P \leqq 0.05$ ** : $P \leqq 0.01$ Test of Dunnett

APPENDIX B 4-2

HEMATOLOGY (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : FEMALE

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	8.70± 0.22	16.4± 0.3	45.9± 1.2	52.8± 0.3	18.8± 0.7	35.7± 1.3	817± 53
31 ppm	10	8.84± 0.28	16.2± 0.5	46.7± 1.6	52.8± 0.5	18.4± 0.2	34.8± 0.5	810± 43
63 ppm	10	8.89± 0.21	16.5± 0.3	47.0± 1.3	52.9± 0.5	18.6± 0.3	35.1± 0.6	814± 84
125 ppm	10	8.90± 0.20	16.4± 0.4	47.0± 1.1	52.8± 0.6	18.4± 0.2	35.0± 0.6	844± 54
250 ppm	10	8.62± 0.44	16.2± 0.4	45.7± 2.3	53.0± 0.7	18.8± 0.9	35.5± 1.8	862± 45
500 ppm	8	8.18± 0.29**	15.1± 0.7**	44.3± 1.8	54.1± 0.8**	18.4± 0.3	34.0± 0.4**	862± 79

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	10	3.03± 0.75	0± 0	31± 8	2± 1	0± 0	4± 1	64± 8	0± 0
31 ppm	10	3.63± 1.20	0± 0	29± 6	1± 1	0± 0	4± 2	65± 5	0± 0
63 ppm	10	2.91± 0.47	1± 1	29± 6	2± 1	0± 0	4± 1	65± 7	0± 0
125 ppm	10	3.38± 0.93	0± 0	28± 7	2± 1	0± 0	4± 2	67± 8	0± 0
250 ppm	10	3.32± 1.04	0± 0	26± 6	1± 1	0± 0	4± 1	69± 6	0± 0
500 ppm	8	2.62± 0.83	1± 1	33± 8	2± 1	0± 0	5± 2	61± 8	0± 0

Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$ Test of Dunnett

APPENDIX B 4-3

HEMATOLOGY (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE: MALE

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	9	10.48± 0.22	15.6± 0.3	47.2± 1.5	45.0± 0.6	14.9± 0.2	33.1± 0.6	1414± 101
31 ppm	9	10.31± 0.33	15.4± 0.4	46.5± 1.6	45.1± 0.7	14.9± 0.3	33.1± 0.4	1400± 97
63 ppm	10	10.38± 0.31	15.5± 0.4	46.8± 2.0	45.1± 1.0	14.9± 0.3	33.1± 0.5	1360± 98
125 ppm	10	10.33± 0.19	15.7± 0.3	47.3± 0.9	45.8± 0.5	15.2± 0.2*	33.1± 0.7	1392± 293
250 ppm	10	10.05± 0.18**	15.2± 0.3	46.2± 1.2	46.0± 0.7*	15.1± 0.2	32.9± 0.3	1507± 51
500 ppm	0	-	-	-	-	-	-	-

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	9	1.23± 0.61	0± 1	19± 3	2± 1	0± 0	3± 2	76± 4	0± 0
31 ppm	9	0.97± 0.71	0± 1	16± 4	1± 1	0± 0	3± 1	80± 4	0± 0
63 ppm	10	1.35± 0.84	1± 1	19± 6	1± 1	0± 0	3± 2	76± 7	0± 0
125 ppm	10	1.20± 0.80	1± 1	14± 6	2± 2	0± 0	2± 1	82± 7	0± 0
250 ppm	10	1.37± 0.82	1± 1	16± 5	2± 2	0± 0	2± 1	79± 6	0± 0
500 ppm	0	-	-	-	-	-	-	-	-

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett

(HCL071)

APPENDIX B 4-4

HEMATOLOGY (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	10.38± 0.25	15.8± 0.5	46.9± 1.2	45.1± 0.7	15.2± 0.2	33.6± 0.4	1304± 96
31 ppm	10	10.54± 0.37	15.9± 0.5	47.5± 2.0	45.0± 0.7	15.1± 0.2	33.6± 0.9	1326± 114
63 ppm	10	10.46± 0.21	16.0± 0.2	47.5± 1.3	45.4± 0.7	15.3± 0.3	33.7± 0.9	1271± 93
125 ppm	10	10.27± 0.23	15.7± 0.3	46.6± 0.8	45.4± 0.5	15.3± 0.2	33.6± 0.3	1368± 117
250 ppm	10	10.01± 0.33*	15.3± 0.4*	46.2± 1.6	46.2± 0.8**	15.3± 0.2	33.2± 0.5	1374± 64
500 ppm	1	9.66± 0.00 ?	14.5± 0.0 ?	45.3± 0.0 ?	46.9± 0.0 ?	15.0± 0.0 ?	32.0± 0.0 ?	1426± 0 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	10	0.71± 0.65	1± 1	20± 7	0± 1	0± 0	2± 1	77± 6	0± 0
31 ppm	10	0.99± 0.87	1± 1	22± 7	1± 1	0± 0	3± 2	74± 7	0± 0
63 ppm	10	1.32± 1.14	1± 2	19± 3	1± 1	0± 0	2± 2	77± 4	0± 0
125 ppm	10	0.78± 0.52	1± 1	23± 7	1± 1	0± 0	2± 1	74± 7	0± 0
250 ppm	10	1.68± 1.17	1± 1	22± 10	1± 1	0± 0	2± 1	74± 11	0± 0
500 ppm	1	1.48± 0.00 ?	0± 0 ?	14± 0 ?	2± 0 ?	0± 0 ?	2± 0 ?	82± 0 ?	0± 0 ?

Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$ Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX B 5-1

BIOCHEMISTRY (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : MALE

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ	ALBUMIN g/dℓ	A/G RATIO	T-BILIRUBIN mg/dℓ	GLUCOSE mg/dℓ	T-CHOLESTEROL mg/dℓ	TRIGLYCERIDE mg/dℓ
Control	10	6.8± 0.1	3.9± 0.1	1.4± 0.0	0.22± 0.04	196± 14	54± 7	94± 23
31 ppm	10	6.8± 0.2	4.0± 0.1	1.4± 0.1	0.24± 0.05	199± 15	57± 6	96± 20
63 ppm	10	6.8± 0.2	4.0± 0.1	1.4± 0.0	0.23± 0.05	194± 12	58± 4	106± 25
125 ppm	10	7.0± 0.1*	4.0± 0.2	1.4± 0.1	0.24± 0.04	196± 8	57± 7	111± 31
250 ppm	10	6.9± 0.2	4.1± 0.1	1.4± 0.1	0.22± 0.03	191± 18	61± 3	99± 26
500 ppm	6	7.0± 0.2	4.2± 0.1**	1.5± 0.1*	0.25± 0.04	145± 14**	91± 22**	43± 3*

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CPK IU/ℓ
Control	10	106± 11	79± 17	28± 4	166± 78	324± 25	1± 0	90± 27
31 ppm	10	113± 12	77± 15	28± 6	172± 64	335± 30	1± 0	87± 16
63 ppm	10	116± 9	71± 5	27± 2	141± 39	340± 31	2± 1	85± 8
125 ppm	10	116± 13	73± 9	26± 3	164± 64	320± 26	1± 1	83± 14
250 ppm	10	118± 8	65± 9	24± 4	153± 38	313± 36	2± 1	80± 9
500 ppm	6	152± 38**	77± 23	50± 34	193± 81	263± 19**	2± 1	62± 17

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	10	16.9± 1.5	0.5± 0.1	143± 1	3.2± 0.1	106± 1	10.1± 0.6	5.3± 0.9
31 ppm	10	17.5± 1.3	0.5± 0.0	143± 1	3.3± 0.1	106± 1	10.3± 0.4	5.3± 0.7
63 ppm	10	18.2± 1.2	0.5± 0.1	142± 1	3.4± 0.3	105± 1	10.4± 0.2	5.7± 0.9
125 ppm	10	17.9± 1.7	0.5± 0.0	143± 1	3.3± 0.1	104± 1**	10.4± 0.2	5.7± 1.1
250 ppm	10	17.5± 1.2	0.5± 0.0	142± 1	3.5± 0.2*	104± 1**	10.4± 0.1	5.9± 0.8
500 ppm	6	15.6± 1.0	0.4± 0.0	143± 1	3.6± 0.3*	105± 1	10.2± 0.2	5.8± 0.7

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 5-2

BIOCHEMISTRY (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : FEMALE

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ	ALBUMIN g/dℓ	A/G RATIO	T-BILIRUBIN mg/dℓ	GLUCOSE mg/dℓ	T-CHOLESTEROL mg/dℓ	TRIGLYCERIDE mg/dℓ
Control	10	6.5± 0.2	3.8± 0.1	1.4± 0.1	0.29± 0.03	130± 9	73± 6	43± 4
31 ppm	10	6.5± 0.1	3.8± 0.1	1.4± 0.1	0.30± 0.07	135± 15	73± 8	43± 6
63 ppm	10	6.5± 0.1	3.8± 0.1	1.4± 0.0	0.32± 0.10	135± 17	75± 6	42± 7
125 ppm	10	6.5± 0.2	3.8± 0.1	1.4± 0.1	0.31± 0.07	131± 19	76± 5	44± 6
250 ppm	10	6.5± 0.2	3.8± 0.1	1.4± 0.1	0.29± 0.06	128± 15	73± 4	41± 6
500 ppm	8	6.9± 0.3**	4.3± 0.2**	1.7± 0.1**	0.39± 0.19	119± 31	74± 26	39± 8

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CPK IU/ℓ
Control	10	136± 12	76± 11	26± 6	214± 72	244± 25	2± 1	105± 22
31 ppm	10	137± 12	69± 9	24± 5	216± 82	232± 35	2± 1	103± 24
63 ppm	10	138± 12	71± 13	23± 6	262± 127	235± 22	2± 0	112± 30
125 ppm	10	139± 8	70± 12	23± 7	244± 110	226± 25	2± 1	103± 27
250 ppm	10	135± 7	64± 3	20± 1	272± 143	241± 35	1± 0	103± 35
500 ppm	8	131± 41	96± 50	61± 61	454± 299	258± 39	6± 3**	95± 40

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	10	16.7± 1.5	0.5± 0.1	143± 1	3.0± 0.2	108± 2	10.0± 0.1	4.5± 1.2
31 ppm	10	16.4± 1.1	0.5± 0.1	143± 1	3.1± 0.2	108± 1	10.0± 0.2	4.7± 1.2
63 ppm	10	17.0± 1.6	0.5± 0.1	143± 1	3.1± 0.3	108± 1	10.0± 0.2	4.8± 1.0
125 ppm	10	17.5± 1.8	0.5± 0.1	143± 1	3.3± 0.3	107± 2	10.0± 0.2	4.9± 1.0
250 ppm	10	17.9± 1.3	0.5± 0.1	142± 1	3.3± 0.2	106± 2	10.1± 0.2	5.4± 0.8
500 ppm	8	14.9± 2.1	0.4± 0.1	143± 2	3.6± 0.5**	107± 2	10.0± 0.2	5.6± 0.6

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 5-3

BIOCHEMISTRY (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE: MALE

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ	ALBUMIN g/dℓ	A/G RATIO	T-BILIRUBIN mg/dℓ	GLUCOSE mg/dℓ	T-CHOLESTEROL mg/dℓ	TRIGLYCERIDE mg/dℓ
Control	9	5.3± 0.1	2.9± 0.1	1.2± 0.1	0.24± 0.09	213± 59	77± 5	56± 11
31 ppm	9	5.1± 0.2*	2.8± 0.1	1.2± 0.1	0.23± 0.04	186± 38	66± 6*	44± 8
63 ppm	10	5.2± 0.1	2.9± 0.1	1.2± 0.1	0.23± 0.03	194± 41	72± 9	46± 15
125 ppm	10	5.3± 0.1	2.9± 0.1	1.2± 0.1	0.29± 0.10	200± 36	79± 8	44± 6
250 ppm	10	5.4± 0.2	3.0± 0.1	1.3± 0.0	0.24± 0.04	192± 47	92± 11**	44± 7
500 ppm	0	-	-	-	-	-	-	-

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		ALP IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ	
Control	9	49±	5	13±	2	202±	23	182±	17	50±	11	24.1±	2.8	153±	1
31 ppm	9	49±	9	13±	2	205±	36	185±	14	53±	20	25.7±	4.4	154±	2
63 ppm	10	51±	8	13±	3	233±	55	189±	14	85±	96	25.2±	3.7	154±	2
125 ppm	10	45±	6	13±	1	232±	21	196±	27	47±	8	24.8±	5.4	154±	2
250 ppm	10	46±	12	13±	2	231±	48	183±	15	44±	16	22.7±	2.8	154±	2
500 ppm	0	-		-		-		-		-		-		-	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	9	4.2±	0.4	121±	2	8.9±	0.2	7.2±	1.1
31 ppm	9	4.1±	0.4	121±	2	8.6±	0.3*	7.2±	0.9
63 ppm	10	4.4±	0.4	121±	2	8.8±	0.3	7.2±	1.1
125 ppm	10	4.4±	0.3	121±	2	9.0±	0.2	7.2±	1.0
250 ppm	10	4.6±	0.4	122±	1	8.9±	0.2	7.2±	1.3
500 ppm	0	-		-		-		-	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 5-4

BIOCHEMISTRY (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ	ALBUMIN g/dℓ	A/G RATIO	T-BILIRUBIN mg/dℓ	GLUCOSE mg/dℓ	T-CHOLESTEROL mg/dℓ	TRIGLYCERIDE mg/dℓ
Control	10	5.4± 0.2	3.2± 0.1	1.4± 0.1	0.24± 0.04	174± 28	64± 9	32± 8
31 ppm	10	5.5± 0.2	3.2± 0.2	1.4± 0.1	0.28± 0.09	156± 26	71± 8	43± 13
63 ppm	10	5.3± 0.2	3.2± 0.1	1.5± 0.0	0.24± 0.06	167± 35	73± 9*	39± 6
125 ppm	10	5.5± 0.2	3.2± 0.1	1.4± 0.1	0.24± 0.04	154± 35	74± 6*	37± 5
250 ppm	10	5.4± 0.1	3.2± 0.1	1.5± 0.1	0.29± 0.08	150± 30	85± 8**	41± 7
500 ppm	1	5.7± 0.0 ?	3.3± 0.0 ?	1.4± 0.0 ?	0.20± 0.00 ?	173± 0 ?	113± 0 ?	29± 0 ?

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	CPK IU/ℓ	UREA NITROGEN mg/dℓ	SODIUM mEq/ℓ
Control	10	72± 16	16± 3	307± 89	321± 40	120± 94	22.1± 3.1	153± 2
31 ppm	10	65± 14	15± 2	261± 73	304± 62	71± 43	22.3± 4.1	153± 2
63 ppm	10	63± 16	15± 3	260± 106	310± 44	81± 74	22.6± 4.9	153± 1
125 ppm	10	60± 9	15± 1	261± 77	316± 26	60± 29	22.7± 3.3	153± 2
250 ppm	10	52± 9**	15± 2	251± 46	276± 35	43± 8**	18.0± 2.4	153± 1
500 ppm	1	40± 0 ?	15± 0 ?	181± 0 ?	346± 0 ?	33± 0 ?	17.3± 0.0 ?	154± 0 ?

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	10	4.4± 0.5	121± 2	8.8± 0.4	6.8± 0.7
31 ppm	10	4.4± 0.3	121± 3	9.1± 0.3	6.8± 1.0
63 ppm	10	4.2± 0.3	119± 2	9.0± 0.3	6.2± 1.0
125 ppm	10	4.4± 0.3	121± 1	9.1± 0.4	6.5± 1.2
250 ppm	10	4.5± 0.3	120± 3	9.2± 0.2	6.6± 0.9
500 ppm	1	4.5± 0.0 ?	119± 0 ?	9.3± 0.0 ?	6.1± 0.0 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX B 6-1

URINALYSIS (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : MALE

STUDY NO. : 0208
ANIMAL : RAT F344
SAMPLING DATE : 013-5
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	1	1	6	2	0		0	5	3	2	0	0		10	0	0	0	0	0		8	1	1	0	0	0		10	0	0	0	
31 ppm	10	0	0	0	7	3	0	0	*	0	6	4	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
63 ppm	10	0	0	0	1	6	2	1		0	4	5	1	0	0		10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	
125 ppm	10	0	0	0	4	1	5	0		0	4	6	0	0	0		10	0	0	0	0	0		8	2	0	0	0	0		10	0	0	0	
250 ppm	10	0	0	0	4	2	3	1		0	2	6	2	0	0		10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	
500 ppm	6	0	0	0	0	2	4	0		0	0	2	2	2	0		6	0	0	0	0	0		4	2	0	0	0	0		6	0	0	0	

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01

Test of CHI SQUARE

(JCL101)

STUDY NO. : 0208
ANIMAL : RAT F344
SAMPLING DATE : 013-5
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
31 ppm	10	10	0	0	0	0		10	0	0	0	0	
63 ppm	10	10	0	0	0	0		10	0	0	0	0	
125 ppm	10	10	0	0	0	0		10	0	0	0	0	
250 ppm	10	10	0	0	0	0		10	0	0	0	0	
500 ppm	6	6	0	0	0	0		6	0	0	0	0	

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX B 6-2

URINALYSIS (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : FEMALE

STUDY NO. : 0208
ANIMAL : RAT F344
SAMPLING DATE : 013-5
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	1	6	3	0		2	5	3	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
31 ppm	10	0	0	0	1	6	2	1		1	8	1	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
63 ppm	10	0	0	0	1	1	8	0		0	8	2	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
125 ppm	10	0	0	0	3	7	0	0		3	6	1	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
250 ppm	10	0	0	0	2	5	3	0		0	9	1	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
500 ppm	8	0	0	2	1	4	1	0		1	3	2	2	0	0		8	0	0	0	0	0		7	1	0	0	0	0		8	0	0	0	

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0208
ANIMAL : RAT F344
SAMPLING DATE : 013-5
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
31 ppm	10	10	0	0	0	0		10	0	0	0	0	
63 ppm	10	10	0	0	0	0		10	0	0	0	0	
125 ppm	10	10	0	0	0	0		10	0	0	0	0	
250 ppm	10	10	0	0	0	0		10	0	0	0	0	
500 ppm	8	8	0	0	0	0		8	0	0	0	0	

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX B 6-3

URINALYSIS (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE : MALE

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-4
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	0	1	4	4	1		0	0	10	0	0	0		10	0	0	0	0	0		1	8	1	0	0	0		9	0	0	1	0	
31 ppm	10	0	0	0	2	1	6	1		0	2	6	2	0	0		10	0	0	0	0	0		0	3	7	0	0	0	*	10	0	0	0	0	
63 ppm	10	0	1	1	2	1	5	0		0	2	6	2	0	0		10	0	0	0	0	0		2	4	4	0	0	0		10	0	0	0	0	
125 ppm	10	0	0	1	0	3	5	1		0	2	7	1	0	0		10	0	0	0	0	0		2	7	1	0	0	0		10	0	0	0	0	
250 ppm	10	0	2	1	2	1	3	1		0	0	8	2	0	0		10	0	0	0	0	0		0	8	2	0	0	0		10	0	0	0	0	
500 ppm	0	-	-	-	-	-	-	-		-	-	-	-	-	-		-	-	-	-	-	-		-	-	-	-	-	-		-	-	-	-	-	

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-4
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
31 ppm	10	10	0	0	0	0	
63 ppm	10	10	0	0	0	0	
125 ppm	10	10	0	0	0	0	
250 ppm	10	10	0	0	0	0	
500 ppm	0	-	-	-	-	-	

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX B 6-4

URINALYSIS (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE : FEMALE

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-4
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	0	5	1	4	0		0	1	9	0	0	0		10	0	0	0	0	0		3	4	3	0	0	0		10	0	0	0	0	
31 ppm	10	0	0	0	3	2	5	0		0	2	6	2	0	0		10	0	0	0	0	0		5	1	4	0	0	0		10	0	0	0	0	
63 ppm	10	0	0	0	5	2	2	1		0	4	5	1	0	0		10	0	0	0	0	0		5	4	1	0	0	0		10	0	0	0	0	
125 ppm	10	0	0	0	0	6	3	1	*	0	3	7	0	0	0		10	0	0	0	0	0		5	5	0	0	0	0		10	0	0	0	0	
250 ppm	10	0	0	0	3	1	4	2		0	2	8	0	0	0		10	0	0	0	0	0		3	3	4	0	0	0		10	0	0	0	0	
500 ppm	1	0	0	1	0	0	0	0	?	0	0	1	0	0	0	?	1	0	0	0	0	0	?	0	0	1	0	0	0	?	1	0	0	0	0	?

Significent difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-4
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
31 ppm	10	10	0	0	0	0	
63 ppm	10	10	0	0	0	0	
125 ppm	10	10	0	0	0	0	
250 ppm	10	10	0	0	0	0	
500 ppm	1	1	0	0	0	0	?

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX B 7-1

GROSS FINDINGS (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : MALE: SACRIFICED ANIMALS

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	31 ppm 10 (%)	63 ppm 10 (%)	125 ppm 10 (%)
lung	mass		1 (10)	0 (0)	0 (0)	0 (0)
gl stomach	ulcer		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		1 (10)	0 (0)	1 (10)	0 (0)

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name	250 ppm	500 ppm
		NO. of Animals	10 (%)	6 (%)
lung	mass		0 (0)	0 (0)
gl stomach	ulcer		0 (0)	2 (33)
liver	herniation		0 (0)	0 (0)

APPENDIX B 7-2

GROSS FINDINGS (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : FEMALE: SACRIFICED ANIMALS

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	31 ppm 10 (%)	63 ppm 10 (%)	125 ppm 10 (%)
gl stomach	ulcer		0 (0)	0 (0)	0 (0)	0 (0)
eye	white		0 (0)	0 (0)	1 (10)	0 (0)

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name	250 ppm	500 ppm
		NO. of Animals	10 (%)	8 (%)
gl stomach	ulcer		0 (0)	2 (25)
eye	white		0 (0)	0 (0)

APPENDIX B 7-3

GROSS FINDINGS (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : MALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	31 ppm 0 (%)	63 ppm 0 (%)	125 ppm 0 (%)
forestomach	ulcer		- (-)	- (-)	- (-)	- (-)
urin bladd	dilated		- (-)	- (-)	- (-)	- (-)
	urine:marked retention		- (-)	- (-)	- (-)	- (-)
abdominal c	ascites		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

Organ	Findings	Group Name NO. of Animals	250 ppm 0 (%)	500 ppm 4 (%)
forestomach	ulcer		- (-)	1 (25)
urin bladd	dilated		- (-)	1 (25)
	urine:marked retention		- (-)	3 (75)
abdominal c	ascites		- (-)	1 (25)

APPENDIX B 7-4

GROSS FINDINGS (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : FEMALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

Organ	Findings	Group Name / NO. of Animals	Control 0 (%)	31 ppm 0 (%)	63 ppm 0 (%)	125 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

Organ	Findings	Group Name	250 ppm	500 ppm
		NO. of Animals	0 (%)	2 (%)
thymus	atrophic		- (-)	1 (50)

APPENDIX B 7-5

GROSS FINDINGS (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE : MALE: SACRIFICED ANIMALS

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	31 ppm 10 (%)	63 ppm 10 (%)	125 ppm 10 (%)
spleen	black zone		0 (0)	0 (0)	0 (0)	1 (10)
kidney	hydronephrosis		0 (0)	0 (0)	1 (10)	0 (0)
ureter	dilated		0 (0)	0 (0)	1 (10)	0 (0)

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name	250 ppm	500 ppm
		NO. of Animals	10 (%)	0 (%)
spleen	black zone		0 (0)	- (-)
kidney	hydronephrosis		0 (0)	- (-)
ureter	dilated		0 (0)	- (-)

APPENDIX B 7-6

GROSS FINDINGS (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE : FEMALE: SACRIFICED ANIMALS

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	31 ppm 10 (%)	63 ppm 10 (%)	125 ppm 10 (%)
spleen	black zone		1 (10)	0 (0)	1 (10)	0 (0)
ovary	cyst		0 (0)	1 (10)	1 (10)	0 (0)

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name	250 ppm	500 ppm
		NO. of Animals	10 (%)	1 (%)
spleen	black zone		0 (0)	1 (100)
ovary	cyst		0 (0)	0 (0)

APPENDIX B 7-7

GROSS FINDINGS (THIRTEEN-WEEK STUDY : SUMMARY),

MOUSE : MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

Organ	Findings	Group Name / NO. of Animals	Control 0 (%)	31 ppm 0 (%)	63 ppm 0 (%)	125 ppm 0 (%)
lung	red		- (-)	- (-)	- (-)	- (-)
liver	turbid		- (-)	- (-)	- (-)	- (-)
	white zone		- (-)	- (-)	- (-)	- (-)
	red zone		- (-)	- (-)	- (-)	- (-)
testis	atrophic		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

Organ	Findings	Group Name NO. of Animals	250 ppm 0 (%)	500 ppm 10 (%)
lung	red		- (-)	1 (10)
liver	turbid		- (-)	1 (10)
	white zone		- (-)	3 (30)
	red zone		- (-)	2 (20)
testis	atrophic		- (-)	1 (10)

APPENDIX B 7-8

GROSS FINDINGS (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	31 ppm 0 (%)	63 ppm 0 (%)	125 ppm 0 (%)
liver	white zone		- (-)	- (-)	- (-)	- (-)
kidney	hydronephrosis		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

Organ	Findings	Group Name NO. of Animals	250 ppm 0 (%)	500 ppm 9 (%)
liver	white zone		- (-)	1 (11)
kidney	hydronephrosis		- (-)	1 (11)

APPENDIX B 8-1

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),ABSOLUTE

RAT : MALE

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	311± 22	0.275± 0.032	0.054± 0.003	2.899± 0.094	0.954± 0.034	1.004± 0.059
31 ppm	10	295± 20	0.247± 0.014	0.052± 0.003	2.868± 0.101	0.915± 0.042	0.951± 0.068
63 ppm	10	298± 16	0.266± 0.033	0.051± 0.003	2.894± 0.119	0.942± 0.067	0.963± 0.051
125 ppm	10	293± 21	0.242± 0.035*	0.051± 0.003	2.903± 0.113	0.921± 0.079	0.953± 0.050
250 ppm	10	281± 12**	0.226± 0.018**	0.048± 0.004**	2.857± 0.078	0.903± 0.042	0.941± 0.039*
500 ppm	6	160± 14**	0.087± 0.019**	0.045± 0.003**	1.669± 0.317**	0.708± 0.049**	0.780± 0.042**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HCL040)

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.793± 0.102	0.518± 0.023	7.796± 0.737	1.877± 0.040
31 ppm	10	1.778± 0.129	0.498± 0.035	7.562± 0.654	1.865± 0.045
63 ppm	10	1.856± 0.110	0.515± 0.030	7.761± 0.469	1.864± 0.037
125 ppm	10	1.941± 0.101*	0.514± 0.037	7.849± 0.601	1.878± 0.035
250 ppm	10	1.991± 0.101**	0.509± 0.033	7.933± 0.480	1.822± 0.029**
500 ppm	6	1.631± 0.115*	0.314± 0.040**	5.844± 0.619**	1.575± 0.039**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 8-2

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),ABSOLUTE

RAT : FEMALE

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	171± 7	0.202± 0.019	0.053± 0.003	0.106± 0.019	0.623± 0.032	0.746± 0.040
31 ppm	10	173± 9	0.198± 0.017	0.054± 0.006	0.103± 0.012	0.616± 0.049	0.752± 0.035
63 ppm	10	171± 10	0.208± 0.014	0.051± 0.005	0.097± 0.010	0.620± 0.025	0.741± 0.050
125 ppm	10	170± 11	0.199± 0.018	0.052± 0.005	0.096± 0.009	0.604± 0.057	0.736± 0.029
250 ppm	10	165± 8	0.191± 0.017	0.051± 0.004	0.102± 0.010	0.624± 0.034	0.727± 0.033
500 ppm	8	115± 14**	0.094± 0.027**	0.049± 0.006	0.062± 0.009**	0.548± 0.039**	0.658± 0.031**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.122± 0.044	0.350± 0.025	4.009± 0.194	1.752± 0.043
31 ppm	10	1.140± 0.071	0.350± 0.025	4.085± 0.329	1.739± 0.042
63 ppm	10	1.131± 0.059	0.340± 0.020	4.003± 0.231	1.721± 0.032
125 ppm	10	1.163± 0.063	0.346± 0.027	3.987± 0.222	1.720± 0.049
250 ppm	10	1.183± 0.034	0.356± 0.030	4.141± 0.128	1.712± 0.041
500 ppm	8	1.244± 0.043**	0.240± 0.021**	4.508± 0.377*	1.528± 0.032**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 8-3

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),ABSOLUTE

MOUSE: MALE

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	28.6± 2.8	0.033± 0.004	0.009± 0.002	0.197± 0.040	0.151± 0.011	0.153± 0.009
31 ppm	10	27.2± 2.3	0.031± 0.006	0.009± 0.002	0.201± 0.028	0.149± 0.018	0.153± 0.014
63 ppm	10	27.2± 2.5	0.030± 0.006	0.009± 0.002	0.211± 0.021	0.147± 0.010	0.152± 0.007
125 ppm	10	25.8± 1.7	0.030± 0.003	0.009± 0.001	0.192± 0.037	0.141± 0.013	0.150± 0.009
250 ppm	10	26.3± 1.2	0.029± 0.005	0.010± 0.002	0.196± 0.025	0.140± 0.015	0.149± 0.009
500 ppm	0	-	-	-	-	-	-

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.428± 0.022	0.048± 0.007	1.131± 0.077	0.437± 0.011
31 ppm	10	0.435± 0.032	0.047± 0.006	1.130± 0.097	0.442± 0.013
63 ppm	10	0.504± 0.241	0.049± 0.010	1.119± 0.062	0.440± 0.010
125 ppm	10	0.395± 0.030*	0.047± 0.006	1.039± 0.100	0.433± 0.016
250 ppm	10	0.419± 0.020	0.041± 0.003*	1.047± 0.067	0.433± 0.008
500 ppm	0	-	-	-	-

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 8-4

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),ABSOLUTE

MOUSE: FEMALE

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	20.7± 1.3	0.038± 0.008	0.011± 0.002	0.024± 0.006	0.129± 0.016	0.146± 0.010
31 ppm	10	21.0± 1.7	0.039± 0.007	0.011± 0.002	0.025± 0.007	0.130± 0.014	0.147± 0.011
63 ppm	10	20.7± 1.2	0.038± 0.007	0.011± 0.002	0.029± 0.007	0.129± 0.015	0.148± 0.013
125 ppm	10	20.3± 1.1	0.036± 0.006	0.010± 0.002	0.026± 0.007	0.114± 0.006	0.151± 0.015
250 ppm	10	21.1± 0.9	0.036± 0.006	0.010± 0.001	0.026± 0.007	0.114± 0.007*	0.147± 0.007
500 ppm	1	19.1± 0.0 ?	0.036± 0.000 ?	0.010± 0.000 ?	0.020± 0.000 ?	0.116± 0.000 ?	0.134± 0.000 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.294± 0.017	0.054± 0.007	0.884± 0.083	0.452± 0.017
31 ppm	10	0.291± 0.013	0.056± 0.008	0.903± 0.087	0.445± 0.015
63 ppm	10	0.288± 0.017	0.053± 0.009	0.902± 0.071	0.453± 0.013
125 ppm	10	0.281± 0.023	0.046± 0.005	0.854± 0.064	0.446± 0.016
250 ppm	10	0.289± 0.021	0.045± 0.004*	0.854± 0.053	0.435± 0.013
500 ppm	1	0.281± 0.000 ?	0.043± 0.000 ?	0.903± 0.000 ?	0.443± 0.000 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX B 9-1

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),RELATIVE

RAT : MALE

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	311± 22	0.089± 0.010	0.018± 0.002	0.937± 0.060	0.308± 0.018	0.324± 0.016
31 ppm	10	295± 20	0.084± 0.006	0.018± 0.002	0.976± 0.059	0.311± 0.015	0.323± 0.014
63 ppm	10	298± 16	0.089± 0.008	0.017± 0.001	0.971± 0.043	0.316± 0.013	0.323± 0.012
125 ppm	10	293± 21	0.082± 0.009	0.018± 0.002	0.994± 0.043	0.315± 0.013	0.326± 0.015
250 ppm	10	281± 12**	0.081± 0.006	0.017± 0.001	1.019± 0.030	0.322± 0.013	0.335± 0.008
500 ppm	6	160± 14**	0.054± 0.009**	0.029± 0.003**	1.052± 0.229	0.443± 0.025**	0.489± 0.032**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.578± 0.020	0.167± 0.007	2.507± 0.097	0.606± 0.034
31 ppm	10	0.603± 0.020	0.169± 0.007	2.564± 0.054	0.635± 0.042
63 ppm	10	0.622± 0.024	0.173± 0.006	2.600± 0.046	0.626± 0.031
125 ppm	10	0.664± 0.023**	0.176± 0.010	2.682± 0.107*	0.644± 0.039
250 ppm	10	0.710± 0.014**	0.181± 0.009**	2.826± 0.078**	0.650± 0.028
500 ppm	6	1.021± 0.065**	0.196± 0.016**	3.648± 0.191**	0.989± 0.068**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 9-2

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),RELATIVE

RAT : FEMALE

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	171± 7	0.119± 0.009	0.031± 0.002	0.062± 0.010	0.365± 0.026	0.437± 0.011
31 ppm	10	173± 9	0.115± 0.012	0.031± 0.003	0.060± 0.008	0.356± 0.017	0.436± 0.022
63 ppm	10	171± 10	0.122± 0.009	0.030± 0.002	0.057± 0.005	0.364± 0.019	0.434± 0.018
125 ppm	10	170± 11	0.117± 0.008	0.031± 0.004	0.056± 0.005	0.355± 0.022	0.434± 0.021
250 ppm	10	165± 8	0.116± 0.010	0.031± 0.003	0.062± 0.006	0.379± 0.029	0.441± 0.019
500 ppm	8	115± 14**	0.081± 0.018**	0.043± 0.006**	0.054± 0.005	0.481± 0.052**	0.578± 0.064**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.657± 0.018	0.205± 0.014	2.347± 0.085	1.026± 0.026
31 ppm	10	0.660± 0.021	0.203± 0.011	2.363± 0.094	1.010± 0.060
63 ppm	10	0.662± 0.030	0.199± 0.008	2.342± 0.054	1.010± 0.056
125 ppm	10	0.685± 0.025	0.204± 0.012	2.349± 0.113	1.016± 0.076
250 ppm	10	0.719± 0.027**	0.216± 0.013	2.516± 0.112*	1.040± 0.042
500 ppm	8	1.095± 0.140**	0.210± 0.015	3.939± 0.236**	1.344± 0.149**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 9-3

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),RELATIVE

MOUSE: MALE

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	28.6± 2.8	0.117± 0.017	0.032± 0.008	0.698± 0.159	0.533± 0.055	0.540± 0.054
31 ppm	10	27.2± 2.3	0.114± 0.018	0.033± 0.005	0.740± 0.109	0.547± 0.057	0.563± 0.051
63 ppm	10	27.2± 2.5	0.111± 0.017	0.034± 0.006	0.776± 0.065	0.545± 0.057	0.559± 0.038
125 ppm	10	25.8± 1.7	0.116± 0.013	0.033± 0.005	0.740± 0.127	0.546± 0.055	0.583± 0.032
250 ppm	10	26.3± 1.2	0.111± 0.016	0.037± 0.008	0.748± 0.091	0.533± 0.039	0.567± 0.030
500 ppm	0	-	-	-	-	-	-

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.508± 0.125	0.169± 0.021	3.987± 0.404	1.544± 0.161
31 ppm	10	1.601± 0.076	0.172± 0.019	4.152± 0.159	1.631± 0.118
63 ppm	10	1.884± 1.023	0.183± 0.044	4.124± 0.235	1.626± 0.132
125 ppm	10	1.531± 0.086	0.182± 0.020	4.021± 0.255	1.683± 0.126
250 ppm	10	1.596± 0.091	0.156± 0.014	3.988± 0.202	1.651± 0.064
500 ppm	0	-	-	-	-

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 9-4

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),RELATIVE

MOUSE: FEMALE

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	20.7± 1.3	0.183± 0.031	0.054± 0.009	0.117± 0.025	0.624± 0.076	0.703± 0.028
31 ppm	10	21.0± 1.7	0.188± 0.034	0.055± 0.010	0.119± 0.029	0.620± 0.033	0.702± 0.025
63 ppm	10	20.7± 1.2	0.184± 0.030	0.054± 0.007	0.137± 0.027	0.623± 0.061	0.712± 0.039
125 ppm	10	20.3± 1.1	0.175± 0.028	0.052± 0.010	0.126± 0.029	0.563± 0.046	0.747± 0.061
250 ppm	10	21.1± 0.9	0.171± 0.025	0.049± 0.007	0.124± 0.036	0.539± 0.024**	0.700± 0.038
500 ppm	1	19.1± 0.0 ?	0.188± 0.000 ?	0.052± 0.000 ?	0.105± 0.000 ?	0.607± 0.000 ?	0.702± 0.000 ?

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.418± 0.074	0.259± 0.025	4.255± 0.200	2.183± 0.123
31 ppm	10	1.393± 0.098	0.264± 0.026	4.300± 0.214	2.130± 0.166
63 ppm	10	1.393± 0.046	0.255± 0.035	4.354± 0.200	2.192± 0.112
125 ppm	10	1.386± 0.095	0.226± 0.018*	4.217± 0.163	2.207± 0.074
250 ppm	10	1.373± 0.117	0.216± 0.018**	4.052± 0.154	2.067± 0.082
500 ppm	1	1.471± 0.000 ?	0.225± 0.000 ?	4.728± 0.000 ?	2.319± 0.000 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX B 10-1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10 1 (%)	2 (%)	3 (%)	4 (%)	31 ppm 10 1 (%)	2 (%)	3 (%)	4 (%)	63 ppm 10 1 (%)	2 (%)	3 (%)	4 (%)	125 ppm 10 1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<10>				<10>				<10>				<10>			
	degeneration:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
trachea			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
lung			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	osseous metaplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	epidermal cyst		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	250 ppm				500 ppm			
		No. of Animals on Study	10				6			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				< 6>			
	degeneration:olfactory epithelium		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
trachea			<10>				< 6>			
	lymphocytic infiltration		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<10>				< 6>			
	lymphocytic infiltration		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	osseous metaplasia		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	epidermal cyst		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]										
spleen			<10>				< 6>			
	deposit of hemosiderin		10	0	0	0	0	6	0	0 **
			(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				31 ppm				63 ppm				125 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Circulatory system]																		
heart			<10>				<10>				<10>				<10>			
	granulation		0	0	0	0	2	0	0	0	3	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
stomach			<10>				<10>				<10>				<10>			
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion:glandular stomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<10>				<10>				<10>				<10>			
	herniation		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	degeneration:central		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	250 ppm				500 ppm			
		No. of Animals on Study	10				6			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Circulatory system]										
heart			<10>				< 6>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]										
stomach			<10>				< 6>			
	hyperplasia:forestomach		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(17)	(0)	(0)	(0)
	erosion:glandular stomach		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(33)	(0)	(0)	(0)
liver			<10>				< 6>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	degeneration:central		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(33)	(0)	(0)	(0)
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				31 ppm				63 ppm				125 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	basophilic change		2	0	0	0	1	0	0	0	2	0	0	0	3	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
	eosinophilic body		0	5	5	0	0	9	1	0	0	5	5	0	0	4	6	0
			(0)	(50)	(50)	(0)	(0)	(90)	(10)	(0)	(0)	(50)	(50)	(0)	(0)	(40)	(60)	(0)
	sclerose:glomerulus		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	increased basophility:proximal tubule straight		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]																		
testis			<10>				<10>				<10>				<10>			
	germ cell necrosis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	250 ppm				500 ppm			
		No. of Animals on Study	10				6			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
kidney			<10>				< 6>			
	basophilic change		3	0	0	0	5	0	0	0
			(30)	(0)	(0)	(0)	(83)	(0)	(0)	(0)
	eosinophilic body		0	4	6	0	3	2	0	0 *
			(0)	(40)	(60)	(0)	(50)	(33)	(0)	(0)
	sclerose:glomerulus		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	increased basophility:proximal tubule straight		0	0	0	0	5	0	0	0 **
			(0)	(0)	(0)	(0)	(83)	(0)	(0)	(0)
[Endocrine system]										
pituitary			<10>				< 6>			
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]										
testis			<10>				< 6>			
	germ cell necrosis		0	0	0	0	5	1	0	0 **
			(0)	(0)	(0)	(0)	(83)	(17)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name	Control				31 ppm				63 ppm				125 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Nervous system]																		
brain			<10>				<10>				<10>				<10>			
	degeneration:granular cell		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spinal cord			<10>				<10>				<10>				<10>			
	cyst		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Special sense organs/appandage]																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		1	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	250 ppm				500 ppm			
		No. of Animals on Study	10				6			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Nervous system]										
brain			<10>				< 6>			
	degeneration:granular cell		0 (0)	0 (0)	0 (0)	0 (0)	6 (100)	0 (0)	0 (0)	0 (0) **
spinal cord			<10>				< 6>			
	cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Special sense organs/appandage]										
Harder gl			<10>				< 6>			
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX B 10-2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

Organ	Findings	Group Name	Control				31 ppm				63 ppm				125 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<10>				<10>				<10>				<10>			
	inflammation		2 (20)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)
	degeneration:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
lung			<10>				<10>				<10>				<10>			
	osseous metaplasia		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		0 (0)	3 (30)	0 (0)	0 (0)	1 (10)	1 (10)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	4 (40)	1 (10)	0 (0)	0 (0)
lymph node			<10>				<10>				<10>				<10>			
	granulation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	7 (70)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	250 ppm				500 ppm			
		No. of Animals on Study	10				8			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				< 8>			
	inflammation		2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	degeneration:olfactory epithelium		0	0	0	0	4	0	0	0 *
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
lung			<10>				< 8>			
	osseous metaplasia		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(13)	(0)	(0)	(0)
[Hematopoietic system]										
bone marrow			<10>				< 8>			
	granulation		1	2	0	0	1	0	0	0
			(10)	(20)	(0)	(0)	(13)	(0)	(0)	(0)
lymph node			<10>				< 8>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				< 8>			
	deposit of hemosiderin		10	0	0	0	3	5	0	0 *
			(100)	(0)	(0)	(0)	(38)	(63)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				31 ppm				63 ppm				125 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Circulatory system]																		
heart			<10>				<10>				<10>				<10>			
	myocardial degeneration		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
stomach			<10>				<10>				<10>				<10>			
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion:glandular stomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<10>				<10>				<10>				<10>			
	degeneration:central		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		1	0	0	0	2	0	0	0	2	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	basophilic change		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Grade	250 ppm 10 1 (%)	2 (%)	3 (%)	4 (%)	500 ppm 8 1 (%)	2 (%)	3 (%)	4 (%)
[Circulatory system]										
heart			<10>				< 8>			
	myocardial degeneration		0 (0)	0 (0)	0 (0)	0 (0)	1 (13)	0 (0)	0 (0)	0 (0)
[Digestive system]										
stomach			<10>				< 8>			
	hyperplasia:forestomach		0 (0)	0 (0)	0 (0)	0 (0)	1 (13)	0 (0)	0 (0)	0 (0)
	erosion:glandular stomach		0 (0)	0 (0)	0 (0)	0 (0)	2 (25)	0 (0)	0 (0)	0 (0)
liver			<10>				< 8>			
	degeneration:central		0 (0)	0 (0)	0 (0)	0 (0)	4 (50)	0 (0)	0 (0)	0 * (0)
	granulation		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Urinary system]										
kidney			<10>				< 8>			
	basophilic change		0 (0)	0 (0)	0 (0)	0 (0)	2 (25)	2 (25)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				31 ppm				63 ppm				125 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	mineralization:cortico-medullary junction		5	0	0	0	7	0	0	0	6	0	0	0	7	0	0	0
			(50)	(0)	(0)	(0)	(70)	(0)	(0)	(0)	(60)	(0)	(0)	(0)	(70)	(0)	(0)	(0)
	mineralization:papilla		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	sclerose:glomerulus		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	increased basophility:proximal tubule straight		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			<10>				<10>				<10>				<10>			
	degeneration		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	250 ppm				500 ppm			
		No. of Animals on Study	10				8			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
kidney			<10>				< 8>			
	mineralization:cortico-medullary junction		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(25)	(0)	(0)	(0)
	sclerose:glomerulus		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(25)	(0)	(0)	(0)
	increased basophility:proximal tubule straight		0	0	0	0	8	0	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Endocrine system]										
pituitary			<10>				< 8>			
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			<10>				< 8>			
	degeneration		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(13)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				31 ppm				63 ppm				125 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
thyroid			<10>				<10>				<10>				<10>			
	ultimibranchial body remanet		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Nervous system]																		
brain			<10>				<10>				<10>				<10>			
	degeneration:granular cell		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]																		
eye			<10>				<10>				<10>				<10>			
	cataract		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		2	0	0	0	2	0	0	0	1	1	0	0	1	1	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(10)	(0)	(0)	(10)	(10)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	250 ppm				500 ppm			
		No. of Animals on Study	10				8			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]										
thyroid			<10>				< 8>			
	ultimibranchial body remanet		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Nervous system]										
brain			<10>				< 8>			
	degeneration:granular cell		0	0	0	0	5	0	0	0 *
			(0)	(0)	(0)	(0)	(63)	(0)	(0)	(0)
[Special sense organs/appandage]										
eye			<10>				< 8>			
	cataract		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl			<10>				< 8>			
	lymphocytic infiltration		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX B 10-3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

RAT : MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

Organ	Findings	Group Name	Control				31 ppm				63 ppm				125 ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			< 0>				< 0>				< 0>				< 0>			
	degeneration:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
lung			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Hematopoietic system]																		
spleen			< 0>				< 0>				< 0>				< 0>			
	deposit of hemosiderin		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Digestive system]																		
stomach			< 0>				< 0>				< 0>				< 0>			
	ulcer:forestomach		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	hyperplasia:forestomach		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	250 ppm				500 ppm			
		No. of Animals on Study	0				4			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]										
nasal cavit			< 0>				< 4>			
	degeneration:olfactory epithelium		- (-)	- (-)	- (-)	- (-)	1 (25)	0 (0)	0 (0)	0 (0)
lung			< 0>				< 4>			
	congestion		- (-)	- (-)	- (-)	- (-)	1 (25)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]										
spleen			< 0>				< 4>			
	deposit of hemosiderin		- (-)	- (-)	- (-)	- (-)	0 (0)	4 (100)	0 (0)	0 (0)
[Digestive system]										
stomach			< 0>				< 4>			
	ulcer:forestomach		- (-)	- (-)	- (-)	- (-)	1 (25)	0 (0)	0 (0)	0 (0)
	hyperplasia:forestomach		- (-)	- (-)	- (-)	- (-)	1 (25)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Grade	Control 0				31 ppm 0				63 ppm 0				125 ppm 0			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver		< 0>																
	necrosis:central		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Urinary system]																		
kidney		< 0>																
	basophilic change		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	tubular necrosis:proximale tubule		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Reproductive system]																		
testis		< 0>																
	germ cell necrosis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Nervous system]																		
brain		< 0>																
	degeneration:granular cell		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

STUDY NO. : 0208
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

Organ	Findings	Group Name	250 ppm				500 ppm			
		No. of Animals on Study	0				4			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			< 0>				< 4>			
	necrosis:central		-	-	-	-	0	2	0	0
			(-)	(-)	(-)	(-)	(0)	(50)	(0)	(0)
[Urinary system]										
kidney			< 0>				< 4>			
	basophilic change		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(25)	(0)	(0)	(0)
	tubular necrosis:proximale tubule		-	-	-	-	1	3	0	0
			(-)	(-)	(-)	(-)	(25)	(75)	(0)	(0)
[Reproductive system]										
testis			< 0>				< 4>			
	germ cell necrosis		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(25)	(0)	(0)	(0)
[Nervous system]										
brain			< 0>				< 4>			
	degeneration:granular cell		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(25)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX B 10-4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

Organ	Findings	Group Name	Control				31 ppm				63 ppm				125 ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
lung			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Hematopoietic system]																		
spleen			< 0>				< 0>				< 0>				< 0>			
	deposit of hemosiderin		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Urinary system]																		
kidney			< 0>				< 0>				< 0>				< 0>			
	tubular necrosis:proximale tubule		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	250 ppm				500 ppm			
		No. of Animals on Study	0				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
lung			< 0>				< 2>			
	congestion		-	-	-	-	2	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
[Hematopoietic system]										
spleen			< 0>				< 2>			
	deposit of hemosiderin		-	-	-	-	2	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
[Urinary system]										
kidney			< 0>				< 2>			
	tubular necrosis:proximale tubule		-	-	-	-	0	0	2	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX B 10-5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

MOUSE: MALE : SACRIFICED ANIMALS

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name	Control				31 ppm				63 ppm				125 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<10>				<10>				<10>				<10>			
	eosinophilic change:olfactory epithelium		1	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	eosinophilic change:respiratory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
lung			<10>				<10>				<10>				<10>			
	hemorrhage		0	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]																		
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
[Digestive system]																		
stomach			<10>				<10>				<10>				<10>			
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0 *
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	250 ppm				500 ppm			
		No. of Animals on Study	10				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				< 0>			
	eosinophilic change:olfactory epithelium		1	0	0	0	-	-	-	-
			(10)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	eosinophilic change:respiratory epithelium		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
lung			<10>				< 0>			
	hemorrhage		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Hematopoietic system]										
spleen			<10>				< 0>			
	deposit of melanin		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Digestive system]										
stomach			<10>				< 0>			
	hyperplasia:forestomach		4	6	0	0 **	-	-	-	-
			(40)	(60)	(0)	(0)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				31 ppm				63 ppm				125 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	granulation		2	0	0	0	4	0	0	0	4	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	vacuolization of proximal tubule		9	0	0	0	7	0	0	0	5	0	0	0	1	0	0	0 **
			(90)	(0)	(0)	(0)	(70)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	hydronephrosis		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	250 ppm				500 ppm			
		No. of Animals on Study	10				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			<10>				< 0>			
	granulation		4	0	0	0	-	-	-	-
			(40)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Urinary system]										
kidney			<10>				< 0>			
	vacuolization of proximal tubule		0	0	0	0 **	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	hydronephrosis		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Endocrine system]										
pituitary			<10>				< 0>			
	Rathke pouch		1	0	0	0	-	-	-	-
			(10)	(0)	(0)	(0)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX B 10-6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

MOUSE: FEMALE : SACRIFICED ANIMALS

Organ	Findings	Group Name	Control				31 ppm				63 ppm				125 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<10>				<10>				<10>				<10>			
	eosinophilic change:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
[Hematopoietic system]																		
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		3	0	0	0	4	0	0	0	3	0	0	0	2	0	0	0
			(30)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
[Digestive system]																		
stomach			<10>				<10>				<10>				<10>			
	ulcer:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	1	0	0	0	4	4	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(40)	(40)	(0)	(0)
liver			<10>				<10>				<10>				<10>			
	granulation		3	0	0	0	4	1	0	0	1	0	0	0	1	1	0	0
			(30)	(0)	(0)	(0)	(40)	(10)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(10)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	250 ppm				500 ppm				
		No. of Animals on Study	10				1				
		Grade	1	2	3	4	1	2	3	4	
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	
[Respiratory system]											
nasal cavit			<10>				< 1>				
	eosinophilic change:olfactory epithelium		1	0	0	0	0	0	0	0	?
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	
[Hematopoietic system]											
spleen			<10>				< 1>				
	deposit of melanin		4	0	0	0	1	0	0	0	?
			(40)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	
[Digestive system]											
stomach			<10>				< 1>				
	ulcer:forestomach		0	0	0	0	1	0	0	0	?
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	
	hyperplasia:forestomach		3	7	0	0 **	0	1	0	0	?
			(30)	(70)	(0)	(0)	(0)	(100)	(0)	(0)	
liver			<10>				< 1>				
	granulation		2	0	0	0	0	0	0	0	?
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square
? : Significant test is not applied,because No. of data in this group is less than 3.

Organ	Findings	Group Name	Control				31 ppm				63 ppm				125 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	vacuolization of proximal tubule		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	250 ppm				500 ppm			
		No. of Animals on Study	10				1			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]										
kidney			<10>				< 1>			
	vacuolization of proximal tubule		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0) ?
[Endocrine system]										
pituitary			<10>				< 1>			
	Rathke pouch		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0) ?

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square
? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX B 10-7

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

MOUSE: MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 0 1 (%)	Control 0 2 (%)	Control 0 3 (%)	Control 0 4 (%)	31 ppm 0 1 (%)	31 ppm 0 2 (%)	31 ppm 0 3 (%)	31 ppm 0 4 (%)	63 ppm 0 1 (%)	63 ppm 0 2 (%)	63 ppm 0 3 (%)	63 ppm 0 4 (%)	125 ppm 0 1 (%)	125 ppm 0 2 (%)	125 ppm 0 3 (%)	125 ppm 0 4 (%)
[Respiratory system]																		
lung																		
	congestion	< a >		< 0>				< 0>				< 0>				< 0>		
		b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Digestive system]																		
liver																		
	necrosis:central	< a >		< 0>				< 0>				< 0>				< 0>		
		b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	granulation	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Reproductive system]																		
testis																		
	germ cell necrosis	< a >		< 0>				< 0>				< 0>				< 0>		
		b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	250 ppm				500 ppm			
		No. of Animals on Study	0				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
lung			<0>				<10>			
	congestion		-	-	-	-	5	0	0	0
			(-)	(-)	(-)	(-)	(50)	(0)	(0)	(0)
[Digestive system]										
liver			<0>				<10>			
	necrosis:central		-	-	-	-	1	5	1	0
			(-)	(-)	(-)	(-)	(10)	(50)	(10)	(0)
	granulation		-	-	-	-	0	1	2	0
			(-)	(-)	(-)	(-)	(0)	(10)	(20)	(0)
[Reproductive system]										
testis			<0>				<10>			
	germ cell necrosis		-	-	-	-	5	0	0	0
			(-)	(-)	(-)	(-)	(50)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX B 10-8

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

MOUSE: FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0209
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 0 1 (%)	Control 0 2 (%)	Control 0 3 (%)	Control 0 4 (%)	31 ppm 0 1 (%)	31 ppm 0 2 (%)	31 ppm 0 3 (%)	31 ppm 0 4 (%)	63 ppm 0 1 (%)	63 ppm 0 2 (%)	63 ppm 0 3 (%)	63 ppm 0 4 (%)	125 ppm 0 1 (%)	125 ppm 0 2 (%)	125 ppm 0 3 (%)	125 ppm 0 4 (%)
[Respiratory system]																		
lung																		
	congestion	< a >	< 0>				< 0>				< 0>				< 0>			
		b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Digestive system]																		
stomach																		
	hyperplasia:forestomach	< a >	< 0>				< 0>				< 0>				< 0>			
		b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
liver																		
	necrosis:central	< a >	< 0>				< 0>				< 0>				< 0>			
		b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Urinary system]																		
kidney																		
	hydronephrosis	< a >	< 0>				< 0>				< 0>				< 0>			
		b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	250 ppm				500 ppm			
		No. of Animals on Study	0				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
lung			< 0>				< 9>			
	congestion		-	-	-	-	6	0	0	0
			(-)	(-)	(-)	(-)	(67)	(0)	(0)	(0)
[Digestive system]										
stomach			< 0>				< 9>			
	hyperplasia:forestomach		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(11)	(0)	(0)	(0)
liver			< 0>				< 9>			
	necrosis:central		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(11)	(0)	(0)	(0)
[Urinary system]										
kidney			< 0>				< 9>			
	hydronephrosis		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(11)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX B 11-1

IDENTITY AND PURITY OF MEHALLYL CHLORIDE

(THIRTEEN-WEEK STUDIES)

IDENTITY OF METHALLYLCHLORIDE(THIRTEEN-WEEK STUDIES)

Test Substance Lot No.: LKG5978

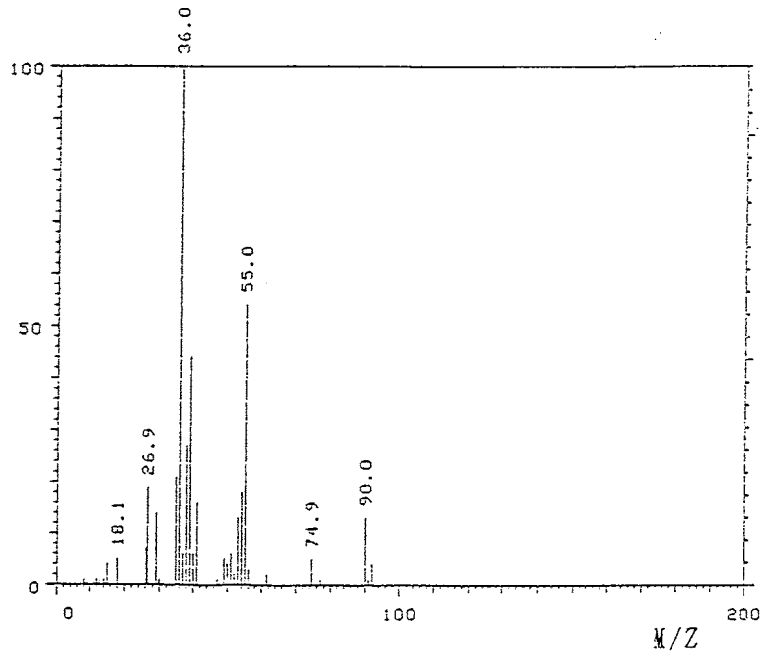
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: Determined Fragment Peak(M/Z)	Literature Value* Fragment Peak(M/Z)
36.0	36
39.0	39
55.0	55
90.0	90

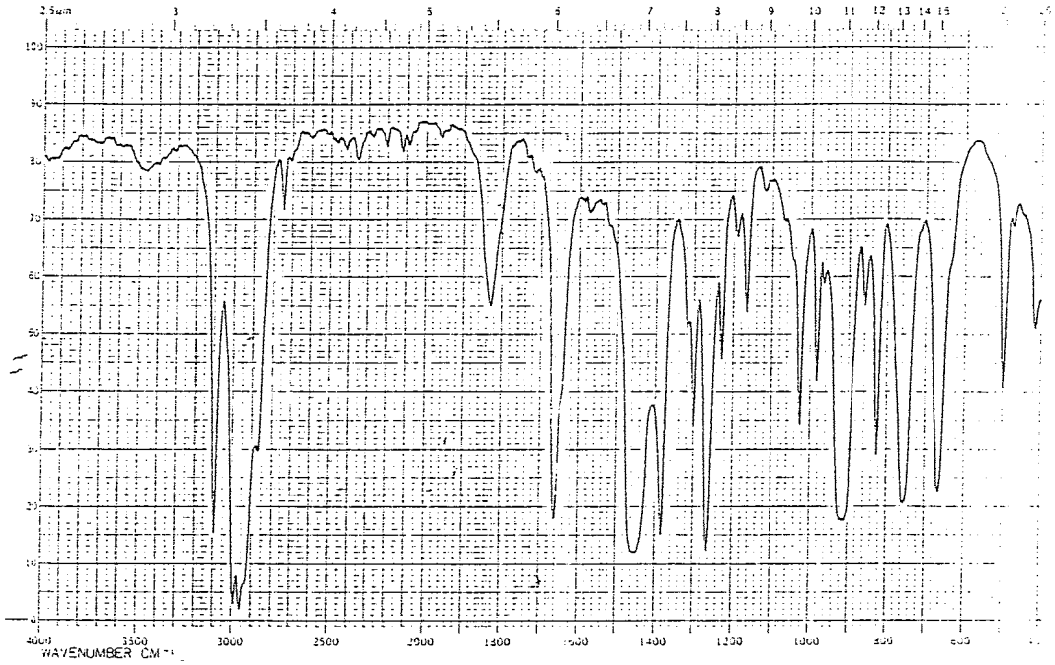
(*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 53.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results:

Determined Value Wave Number(cm^{-1})	Literature Value* Wave Number(cm^{-1})
480～ 520	
640～ 690	640～ 670
720～ 780	720～ 770
800～ 840	800～ 830
880～ 940	880～ 940
970～ 990	960～ 990
1000～1040	1000～1040
1150～1180	1140～1170
1220～1240	1210～1230
1240～1280	1230～1280
1290～1310	1280～1300
1360～1400	1360～1390
1410～1480	1410～1480
1620～1680	1620～1680
1780～1860	1780～1860
2800～3030	2800～3000
3050～3130	3050～3130

(*Performed by the WAKO PURE CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values.
Consequently, the test substance was identified as Methallylchloride.

APPENDIX B 11-2

STABILITY OF METHALLYL CHLORIDE

(THIRTEEN-WEEK STUDIES)

STABILITY OF METHALLYLCHLORIDE(THIRTEEN-WEEK STUDIES)

Test Substance Lot No.: LKG5978

1. Sample: This lot was used from 1992.9.2 to 1992.12.24. Test substance was stored at room temperature .

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results: Infrared spectrum of the test substance agreed with before use and after use.

1992.08.28(date analyzed) Wave Number(cm^{-1})	1992.12.25(date analyzed) Wave Number(cm^{-1})
480～ 520	480～ 520
640～ 690	640～ 690
720～ 780	720～ 780
800～ 840	800～ 840
880～ 940	880～ 940
970～ 990	970～ 990
1000～1040	1000～1040
1150～1180	1150～1180
1220～1240	1220～1240
1240～1280	1240～1280
1290～1310	1290～1310
1360～1400	1360～1400
1410～1480	1410～1480
1620～1680	1620～1680
1780～1860	1780～1860
2800～3030	2800～3030
3050～3130	3050～3130

3. Gas Chromatography

Instrument: Hewlett Packard 5890A

Column: Carbowax 20M(0.2mmϕ × 50m)

Column Temperature: 80°C

Flow Rate: 0.9 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Gas chromatography indicated one major peak(peak No.2) and two impurities(peak No.1,3 < 2% of total area) analyzed at 1992.8.28 and one major peak(peak No.2) and two impurities(peak No.1,3 < 2% of total area) analyzed at 1992.12.25. It was identified only by comparing its gas chromatograph with that of the 1-Chloro-2-methyl-1-propene(peak No.1) and 1,2-Dichloroisobutane (peak No.3) in the Methallylchloride, the amount in the test substance were 1.45% and 0.15% at 1992.8.28. The new treace impurity peak in the test substance analyzed at 1992.12.25 was not detected.

Date	Peak No.	Retention Time(min)	AREA COUNT
1992.08.28	1	4.14	2778
(date analyzed)	2	4.443	173655
	3	5.86	234
1992.12.25	1	4.138	2765
(date analyzed)	2	4.442	172846
	3	5.86	233

4. Conclusions: The results indicated that the test substance did not change when stored in the dark at room temperature during this period(for about 4 months).

APPENDIX B 12-1

CONCENTRATION OF METHALLYL CHLORIDE IN INHALATION CHAMBER

(THIRTEEN-WEEK STUDIES)

CONCENTRATION OF METHALLYL CHLORIDE
IN INHALTION CHAMBER
(RAT: THIRTEEN-WEEK STUDY)

Group Name	Concentration (ppm) Mean ± S.D.
Control	0.0 ± 0.0
31ppm	30.7 ± 0.2
63ppm	62.9 ± 0.3
125ppm	124.4 ± 1.1
250ppm	248.4 ± 2.9
500ppm	497.7 ± 2.2

CONCENTRATION OF METHALLYL CHLORIDE
IN INHALTION CHAMBER
(MOUSE: THIRTEEN-WEEK STUDY)

Group Name	Concentration (ppm) Mean ± S.D.
Control	0.0 ± 0.0
31ppm	31.2 ± 0.2
63ppm	63.1 ± 0.4
125ppm	125.5 ± 0.6
250ppm	250.9 ± 1.1
500ppm	500.9 ± 1.9

APPENDIX B 12-2

ENVIRONMENT OF INHALATION CHAMBER

(THIRTEEN-WEEK STUDIES)

ENVIRONMENT OF INHALATION CHAMBER (RAT: THIRTEEN-WEEK STUDY)

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Room Air Change(time/h) Mean
Control	22.4 ± 0.4	50.9 ± 3.8	212.2 ± 0.4	12.0
31ppm	22.6 ± 0.4	54.0 ± 3.7	211.3 ± 0.5	12.0
63ppm	22.9 ± 0.5	56.9 ± 1.5	210.9 ± 0.5	11.9
125ppm	22.8 ± 0.4	53.6 ± 3.0	211.5 ± 0.4	12.0
250ppm	23.2 ± 0.3	54.8 ± 3.2	211.7 ± 0.8	12.0
500ppm	23.0 ± 0.4	50.3 ± 2.5	212.3 ± 0.5	12.0

ENVIRONMENT OF INHALATION CHAMBER (MOUSE: THIRTEEN-WEEK STUDY)

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Room Air Change(time/h) Mean
Control	22.0 ± 0.5	54.5 ± 4.8	103.9 ± 0.4	12.0
31ppm	22.0 ± 0.4	55.7 ± 3.6	103.7 ± 0.2	12.0
63ppm	21.8 ± 0.3	54.3 ± 3.0	103.3 ± 0.3	11.9
125ppm	21.7 ± 0.3	55.0 ± 3.7	104.1 ± 0.6	12.0
250ppm	22.8 ± 0.1	52.2 ± 2.7	104.0 ± 0.4	12.0
500ppm	21.7 ± 0.1	51.8 ± 2.0	104.4 ± 0.6	12.0

APPENDIX C 1

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS

Item	Method	Unit
Hematology		
Red blood cell	Light scattering method [1]	$\times 10^6 / \mu L$
Hemoglobin	Cyanmethemoglobin method [1]	g/dL
Hematocrit	Calculated as RBC × MCV/10 [1]	%
Mean corpuscular volume (MCV)	Light scattering method [1]	fL
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC × 10 [1]	pg
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct × 10 [1]	g/dL
Platelet	Light scattering method [1]	$\times 10^3 / \mu L$
White blood cell (WBC)	Light scattering method [1]	$\times 10^3 / \mu L$
Differential WBC	Pattern recognition method [2] (May−Grunwald−Giemsa staining)	%
Biochemistry		
Total protein	Biuret method [3]	g/dL
Albumin	BCG method [3]	g/dL
A/G ratio	Calculated as Alb/(TP−Alb) [3]	
T−bilirubin	Michaelson method [3]	mg/dL
Glucose	Enzymatic method (HK·G−6−PDH) [3]	mg/dL
T−cholesterol	Enzymatic method (CEH·COD·POD) [3]	mg/dL
Triglyceride	Enzymatic method (GK·GPO·POD) [3]	mg/dL
Phospholipid	Enzymatic method (PLD·COD·POD) [3]	mg/dL
Glutamic oxaloacetic transaminase (GOT)	Karmen method [3]	IU/L
Glutamic pyruvic transaminase(GPT)	Karmen method [3]	IU/L
Lactate dehydrogenase (LDH)	Wroblewski−LaDue method [3]	IU/L
Alkaline phosphatase (ALP)	GSCC method [3]	IU/L
γ −Glutamyl transpeptidase (G−GTP)	L− γ −Glutamyl−p−nitroanilide substrate method [3]	IU/L
Creatine phosphokinase (CPK)	GSCC method [3]	IU/L
Urea nitrogen	Enzymatic method (Urease ·GLDH) [3]	mg/dL
Creatinine	Jaffe metod [3]	mg/dL
Sodium	Flame photometry [4]	mEq/L
Potassium	Flame photometry [4]	mEq/L
Chloride	Coulometric titration [4]	mEq/L
Calcium	OCPC method 3)	mg/dL
Inorganic phosphorus	Enzymatic method (SPL·PGM·G−6−PDH) [3]	mg/dL
Urinalysis		
pH,Protein,Glucose,Ketone body, Bilirubin, Occult Blood,Urobilinogen	Urinalysis reagent paper metod [5]	

1) Automatic blood cell analyzer (Technicon H·1 : Technicon Instruments Corporation,USA)
2) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi ,Ltd.,Japan)
3) Automatic analyzer (Hitachi 705 : Hitachi ,Ltd.,Japan)
4) Flame photometer (Hitachi 750 : Hitachi ,Ltd.,Japan)
5) Ames reagent strips for urinalysis (Multistix,Uro−Labstix : Miles Sankyo Co.,Ltd.,Japan)

APPENDIX C 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

	TEST ITEM	DECIMAL PLACE	UNIT
HEMATOLOGY	Red blood cell	2	$\times 10^6/\mu L$
	Hemoglobin	1	g/dL
	Hematocrit	1	%
	MCV	1	fL
	MCH	1	pg
	MCHC	1	g/dL
	Platelet	0	$\times 10^3/\mu L$
	White blood cell	2	$\times 10^3/\mu L$
	Differential WBC	0	%
BIOCHEMISTRY	Total protein	1	g/dL
	Albumin	1	g/dL
	A/G ratio	1	—
	T-bilirubin	2	mg/dL
	Glucose	0	mg/dL
	T-cholesterol	0	mg/dL
	Triglyceride	0	mg/dL
	Phospholipid	0	mg/dL
	GOT	0	IU/L
	GPT	0	IU/L
	LDH	0	IU/L
	ALP	0	IU/L
	G-GTP	0	IU/L
	CPK	0	IU/L
	Urea nitrogen	1	mg/dL
	Creatinine	1	mg/dL
	Sodium	0	mEq/L
	Potassium	1	mEq/L
	Chloride	0	mEq/L
	Calcium	1	mg/dL
	Inorganic phosphorus	1	mg/dL